Research Article

Acute Kidney Injury in Weil Disease: Cases Series

Ach Syaiful Ludfi[1,2], Artaria Tjempakasari[3,4]

[1]Internal Medicine Subspecialist Study Program, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Internal Medicine Subspecialist Study Program, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
[3]Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[4]Division of Nephrology, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

ABSTRACT

Leptospirosis is a zoonotic infection with a wide clinical spectrum, ranging from mild illness to severe disease with multi-organ involvement. Acute kidney injury (AKI) is one of the most common complications and may require renal replacement therapy (RRT) in severe cases. We report three cases of leptospirosis-associated AKI in patients with a history of exposure to contaminated water. All patients presented with fever, jaundice, myalgia, and oliguria, accompanied by laboratory findings consistent with AKI. Management included antibiotic therapy, intravenous fluid resuscitation, and supportive care. Diuretics were administered in cases with persistent oliguria. All patients demonstrated significant clinical and laboratory improvement, including recovery of renal function and normalization of urine output. None of the patients required renal replacement therapy. The duration of hospitalization ranged from 5 to 12 days. These cases highlight that early recognition and prompt supportive management may lead to favorable outcomes in leptospirosis-associated AKI without the need for renal replacement therapy.

Keywords: Leptospirosis; Zoonotic Infection; Acute Kidney Injury.

INTRODUCTION

Leptospirosis is a well-known zoonotic disease that is caused by pathogenic Leptospira spp. and is usually spread by drinking water contaminated with animal urine. Indonesia is among the tropical and subtropical areas where the disease is endemic. It exhibits a wide clinical spectrum, ranging from mild, self-limiting illness to severe, life-threatening presentations involving several organ systems—a condition known as Weil's disease (1,2).

Leptospira are aerobic, motile bacteria that reproduce by binary fission; they have a long, spiral structure and do not absorb the Gram stain. They have similar similar characteristics to Gram-negative bacteria, including lipopolysaccharides (LPS) and a double membrane. The peptidoglycan layer is attached to the inner membrane, which sets them apart from ordinary Gram-negative bacteria. Leptospira are members of the spirochetes phylum. There are about 64 species of Leptospira that are either pathogenic or saprophytic. Icterohaemorrhagiae and Copenhageni are the most pertinent serovars, whereas L. interrogans is the most common species among those deemed pathogenic (3).

One of the most frequent and clinically significant complications of severe leptospirosis is AKI. According to recent data from systematic reviews and meta-analyses, 49.2% of patients have AKI, and 14.4% of them need dialysis (4). AKI in leptospirosis is caused by a combination of direct tubular toxicity, an inflammatory response, hemodynamic instability, and other variables such as dehydration and rhabdomyolysis (5,6).

Improving patient outcomes requires early detection and adequate treatment of AKI. Prompt antibiotic medication and supportive care, such as fluid resuscitation and maintaining adequate urine output, are key components of current management strategies. However, there is still a lack of data documenting good renal function recovery without RRT, especially in low-resource settings, and the clinical course and response to conservative management—without dialysis—remain unpredictable (4,6).

In this report, we describe three cases of Weil's disease complicated by AKI that were effectively treated conservatively and did not require dialysis. These instances demonstrate how early and proper supportive care can lead to positive renal outcomes.

METHODS

This study was created as a descriptive case study of patients treated at Citra Husada General Hospital in Jember, Indonesia, who had been diagnosed with AKI linked to leptospirosis. Clinical information, including demographics, clinical presentation, laboratory results, treatment, and results was gathered retrospectively from medical records. Every patient received conventional care, which included supportive care and antimicrobial therapy. Descriptive analysis was used to assess the clinical course and treatment results.

Case Illustration

Case 1

A 25-year-old man was admitted after experiencing fever, jaundice, black tarry stool for the preceding four days, and a single episode of vomiting blood the day before. In recent days, he complained of decreased urine production and severe epigastric pain. He was exposed to the field water because he was a farmer and did not wear shoes when working in the rice fields.

On arrival at the Emergency Department, his vital signs were blood pressure 109/77 mmHg, respiratory rate 24 breaths/min, pulse 97 beats/min, temperature 36.7°C, and oxygen saturation 94% on room air. A physical examination showed calf soreness, jaundice, and scleral icterus. An X-ray of the chest revealed normal results for the heart and lungs. An abdominal ultrasound showing hepatomegaly.

Clinical evaluation revealed systemic involvement and AKI. Ceftriaxone (1 gram every 12 hours), intravenous fluid resuscitation with 0.9% NaCl, and supportive care were all part of the initial therapy. After fluid resuscitation failed to ameliorate oliguria, a diuretic (furosemide) was given. Diuresis improved by second day, with full clinical recovery observed by day four. The patient was discharged on the fifth day after diuresis gradually improved, and dialysis was no longer necessary.

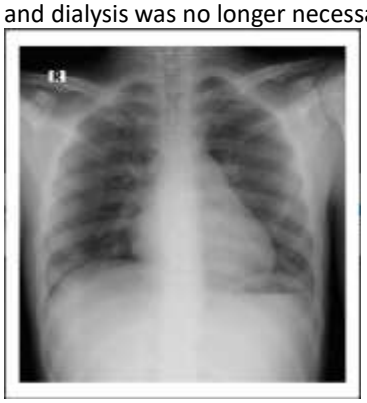

Figure 1. Chest X ray Result of Case 1

Case 2

A 16-year-old boy was admitted after having a fever for a week. He had a high fever for three days, then a lower-grade fever, but two days before he was admitted, he had jaundice along with nausea, vomiting, and tea-colored urine. He also complained of calf and leg pain. The patient had been fishing in a rice paddy without shoes a few days before the onset of the disease, exposing themselves to the paddy water.

The patient's vital signs were as follows when they arrived at the Emergency Department: temperature 37.5°C, oxygen saturation 98% on room air, respiration rate 20 breaths per minute, pulse 100 beats per minute, and blood pressure 75/50 mmHg. A physical examination showed calf soreness, yellowing of the skin, and scleral icterus. An X-ray of the chest revealed normal results for the heart and lungs. An abdominal ultrasound showing normal result.

Initial treatment comprised intravenous fluid resuscitation with 1,000 cc of 0.9% NaCl to increase blood pressure, Ceftriaxone (1 gram every 12 hours), and supportive care. The diuretic furosemide was given since urine production did not improve after fluid resuscitation, despite hemodynamics stabilizing. The patient's diuresis gradually improved, eliminating the need for dialysis; full clinical recovery was noted on the twelfth day; and the patient was discharged on the thirteenth day.

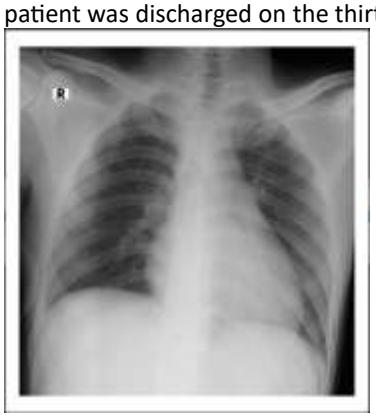

Figure 2. Chest X ray Result of Case 2

Case 3

A 24-year-old man arrived at the emergency room complaining of passing black stools for the previous four days. The bowel movements were mushy, sticky, and asphalt-like, and they happened about five times a day. Before being admitted, he had suffered sporadic fever for seven days. Over the past few days, there had been nausea, vomiting, and epigastric pain in addition to yellowing of the torso, eyes, and palms. Oral consumption decreased. He complained of widespread body and limb pain and tea-colored urine. He had previously meet tainted water because of home flooding in the days leading up to the illness.

Blood pressure of 82/49 mmHg, respiration rate of 20 breaths per minute, pulse of 102 beats per minute, temperature of 36.5°C, and oxygen saturation of 98% on room air were found during the initial evaluation in the Emergency Department. A physical examination revealed calf soreness, yellowing of the skin, and scleral icterus. An X-ray of the chest revealed normal result. An abdominal ultrasound showing hepatomegaly and cholelithiasis The patient was treated with Ceftriaxone (1 gram every 12 hours), a proton pump inhibitor, and supportive care after receiving intravenous fluid resuscitation with 1000 cc of 0.9% NaCl, which initially raised blood pressure. The patient's hemodynamics gradually stabilized, and urine output was sufficient after fluid resuscitation, negating the need for dialysis, and the patient's clinical recovery advanced steadily. The patient was discharged from the hospital on day eleven.

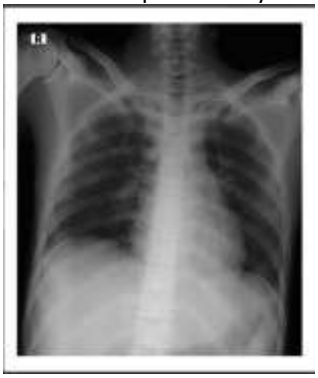

Figure 3. Chest X ray Result of Case 3

Investigations at the time of admission and observation of several days for three cases are depicted in Table 1

Table 1. Clinical and Laboratory Evaluated of Patients with Leptospirosis-Associated AKI

Examination	Case 1		Case 2		Case 3	
	Day 1	Day 4	Day 1	Day 12	Day 1	Day 11
Hemoglobin (g/dL)	14.5	13.1	10.9	11	10.1	9
Hematocrit (%)	43	37	29	31	28	22.8
Leucocyte (x10^3 cell/µL)	23.91	19.43	15.22	8.81	13.77	8.2
Thrombocyte (x10^3 cell/µL)	69.0	161.0	18.0	83.0	29.0	151.0
Natrium (mmol/L)	131	N/A	135	N/A	120	129.7
Kalium (mmol/L)	4.5	N/A	3.9	N/A	2.9	3.3
Chloride (mmol/L)	96	N/A	100	N/A	87	98.3
Calcium (mmol/L)	1.6	N/A	N/A	N/A	2.0	N/A
ALT (U/L)	64	N/A	65	N/A	63	N/A
PT	12.8	N/A	13.7	N/A	13.1	N/A
APTT	28.6	N/A	34.6	N/A	31.3	N/A
AST (U/L)	56	N/A	49	N/A	23	N/A
Albumin (mg/dL)	2.60	N/A	3.2	N/A	3.0	N/A
Creatine (mg/dL)	6.1	0.9	6.1	0.7	2.7	1.2
Urea (mg/dL)	377	38	230	33	150	81
eGFR (mL/min/1.73 m^2)	11	102	12.2	148.6	27.5	69.7
Total Bilirubin (mg/dL)	33.9	N/A	14.2	N/A	48.4	4.64
Conjugated Bilirubin (mg/dL)	28.5	N/A	12.9	N/A	37.30	4.02
IgM Anti-Leptospira	Positif	N/A	Positif	N/A	Positif	N/A

DISCUSSION

Leptospirosis is a serious global public health issue that affects both developing and industrialized countries. The disease typically peaks during the rainy season in tropical regions and rises in summer or fall in temperate zones, according to regional seasonal patterns. The main elements that raise the danger of transmission are significant flooding and heavy rains (7,8).

Leptospira bacteria can infect humans directly or indirectly through contact with the urine, blood, or tissues of infected animals. Bathing or unintentionally coming into contact with freshwater sources—like lakes, rivers, or canals—that have been contaminated by the urine of animals harboring the bacteria can also result in infection (7,9).

Human leptospirosis can cause a wide variety of clinical symptoms, from minor, asymptomatic infections to severe, potentially fatal consequences involving multiple organ failure, including the liver, kidneys, and lungs. Weil's disease, which accounts for 10% of cases, is a severe form of leptospirosis with a high fatality rate. It is characterized by bleeding, renal failure, and liver dysfunction. Early diagnosis and careful care are necessary for patients with Weil's disease (10,11).

Leptospirosis symptoms are highly diverse and vague, depending on both the host (the patient) and the pathogen (the pathogenic bacteria). The majority of infections are probably either subclinical (showing flu-like symptoms) or asymptomatic (12). With an average incubation period of 7 to 12 days, symptoms usually develop 2 to 30 days after exposure. Up to 90% of symptomatic patients exhibit a two-phase (biphasic) pattern. Although it can be challenging to discern between the two phases clinically, this pattern consists of an initial symptomatic leptospiremic phase that lasts five to seven days, followed by an immunological phase during which symptoms may progressively improve as the host's body produces an antibody response. It can be challenging to distinguish the condition from many other febrile illnesses because symptoms typically start with a quick onset of fever, chills, headache, and muscular pain (myalgia) (13,14).

Kidney involvement, which occurs in 10–60% of cases and has a death rate of about 22%, is frequently an early indicator in individuals with Weil's disease (6,15). The direct nephrotoxic effects of bacteria and toxin-induced immunological responses, as well as the indirect effects of the infection—such as dehydration, rhabdomyolysis, and hypoxia brought on by hemodynamic changes—are the two primary mechanisms that cause AKI (5,6).

Leptospira enter the body through the skin or mucous membranes and proceed to the target organs through the bloodstream. The kidneys' proximal tubules are the main targets, along with the liver and lungs (5,6). Tubulointerstitial nephritis, acute tubular necrosis, and a risk of renal fibrosis can result from the bacteria's direct damage to the kidneys after they infect the cells in the renal tubules (6,16).

AKI, which is brought on by the bacteria directly invading renal tissue, especially the proximal tubules, is a serious consequence that is often linked to Leptospira spp. infection. The bacteria use LPS and proteins like OmpL1, LipL41, and LipL32 that are present on proximal tubule epithelial cells. These elements allow the bacteria to attach to and enter the tubular epithelial cells, which in turn activates the complement system and causes direct tissue injury (17,18). Additionally, the current cytokine storm intensifies the pro-inflammatory state and macrophage migration during the acute phase, which damages renal tissue. Additionally, this bacterium lowers the levels of sodium/hydrogen exchanger and aquaporin-1 (AQP-1) on the apical and basolateral membranes and inhibits the performance of the Na+/K+-ATPase pump in the proximal tubules (6,19). This disorder causes the urine to include significant amounts of water and electrolytes (sodium, potassium, calcium, magnesium), resulting in polyuria, which eventually leads to a loss of bodily fluid (hypovolemia) and hypotension (6,20).

The indirect effects of the bacteria, particularly through related hemodynamic abnormalities, can also cause AKI in Weil's disease. Hemodynamic changes in Weil's disease are generally similar to those in ischemic AKI brought on by severe sepsis. The first and most prevalent pattern of hemodynamic change is a decrease in mean arterial pressure (MAP) and systemic vascular resistance (SVR) along with an increase in cardiac index (CI), while pulmonary vascular resistance (PVR) and pulmonary capillary wedge pressure (PCWP) stay normal. Patients with pulmonary problems exhibit the second pattern, which shows high PVR but normal SVR and CI. The final pattern occurs in patients with hyperbilirubinemia, characterized by normal or slightly elevated SVR and decreased CI and MAP, while PVR and PCWP remain unchanged. (18,21). A second indirect cause of AKI is hyperbilirubinemia—frequently observed in leptospirosis—which leads to a decrease in the glomerular filtration rate (GFR) and an impaired ability of the kidneys to concentrate urine. Rhabdomyolysis is another common indirect cause of AKI in Weil's disease, occurring in up to 60% of leptospirosis patients. It induces AKI through mechanisms involving renal vasoconstriction, tubular obstruction, and direct toxicity (18,22).

Patients in all three cases presented with AKI, which was characterized by increased serum creatinine levels and oliguria at hospital admission. All of the patients' renal function considerably improved over time, and none of them needed RRT. These results are clinically significant because research has shown that some patients with Weil’s-associated AKI may worsen and need dialysis, especially if there is extensive systemic involvement or delayed presentation (23).

According to a 2007 study, patients with AKI from Weil's disease who have no other comorbidities may have a higher chance of survival if renal replacement therapy (RRT) is started early and given regularly (24). These findings differ from those of various other large studies. In patients with septic shock in the intensive care unit (ICU), an early RRT strategy was shown to have no beneficial impact on mortality rates or other clinical outcomes when compared to a delayed RRT approach (25–27).

In contrast to previous research, a recent study by Julien et al. found that patients without emergency indications do not benefit from early initiation of RRT in terms of mortality rates or renal recovery. These findings are consistent with those of other significant clinical trials, including IDEAL ICU, AKIKI, and STARRT-AKI. Early RRT initiation may actually have negative effects on the kidneys. Hemodynamic instability associated with renal replacement therapy (HIRRT)—circulatory instability brought on by the dialysis procedure itself—is probably the cause of this. Additionally, the study shows that 75% of patients in the delayed RRT group ultimately did not require RRT. This happened because most patients with AKI caused by leptospirosis reacted favorably to electrolyte correction and fluid resuscitation. This strategy of delaying RRT allows for natural renal recovery, is cost-effective (offering significant advantages in low-income endemic regions), and reduces the risk of catheter-related complications in patients with severe thrombocytopenia (28).

The gradual clinical improvement observed in our patients can be due to early diagnosis and timely beginning of supportive care, notably appropriate fluid resuscitation. To stop more renal ischemia and hasten the restoration of renal function, intravascular volume must be restored (16,29). In cases of persistent oliguria following adequate hydration, diuretics may help increase urine output, although their role remains supportive rather than curative (6,30).

Remarkable findings in these cases include improvements in laboratory markers that coincided with improvements in the clinical condition, such as a decrease serum creatinine and urea levels and the recovery of platelet counts. A prevalent hematological finding in Weil’s disease, thrombocytopenia, has been linked to the severity of the illness and the risk of bleeding (31,32). Previous studies indicate that platelet count correlates with patient prognosis and the resolution of systemic inflammation (33). This is in line with our patients' results, which show that a patient's condition improves when their thrombocytopenia improves.

The results in these cases demonstrate that not all patients with Weil’s disease-associated AKI need early dialysis as compared to previously documented cases. Even in patients who present with severe renal impairment, early conservative therapy can result in a good renal recovery, according to recent data. This is especially critical in resource-constrained settings, where early supportive care is vital to patient outcomes and dialysis access may be limited. Overall, these instances show that effective renal recovery is possible without the need for dialysis, highlighting the need of early identification and proper supportive care for patients with Weil’s disease-associated AKI.

CONCLUSION

There have been three reported cases of Weil’s disease-related AKI. After receiving antibiotics, fluid therapy, and supportive care, the patients' clinical and laboratory parameters improved without the need for RRT. These results demonstrate that Weil’s disease-associated AKI can benefit from early supportive care without the need for RRT.

REFERENCES

1. Abela-Ridder B, Sikkema R, Hartskeerl RA. Estimating the burden of human leptospirosis. Int J Antimicrob Agents. 2010 Nov;36:S5–7. doi:10.1016/j.ijantimicag.2010.06.012
2. Samrot AV, Sean TC, Bhavya KS, Sahithya CS, Chan-drasekaran S, Palanisamy R, et al. Leptospiral Infection, Pathogenesis and Its Diagnosis—A Review. Pathogens. 2021 Feb 1;10(2):145. doi:10.3390/pathogens10020145
3. Gonçalves-de-Albuquerque CF, Cunha CMCD, Castro LVGD, Martins CDA, Barnese MRC, Burth P, et al. Cellular Pathophysiology of Leptospirosis: Role of Na/K-ATPase. Microorganisms. 2023 Jun 29;11(7):1695. doi:10.3390/microorganisms11071695
4. Sethi A, Kumar TP, Vinod KS, Boodman C, Bhat R, Ravindra P, et al. Kidney involvement in leptospirosis: a systematic review and meta-analysis. Infection. 2025 Jun;53(3):785–96. doi:10.1007/s15010-025-02492-1
5. Da Silva Junior G, Srisawat N, Galdino G, Macedo Ê, Pinto J, Farias GN, et al. Acute kidney injury in leptospirosis: Overview and perspectives. Asian Pac J Trop Med. 2018;11(10):549. doi:10.4103/1995-7645.244514

6. Osorio-Rodríguez E, Rodelo-Barrios D, Rebolledo-Maldonado C, Polo-Barranco A, Patiño-Patiño J, Aldana-Roa M, et al. Acute Kidney Injury Associated with Severe Leptospirosis: Fatal Re-Emerging Disease in Latin America. Kidney Dial. 2024 Apr 3;4(2):78–92. doi:10.3390/kidneydial4020006
7. McGrowder D, McGrowder D, Dr. Paul Brown. Clinical and laboratory findings in patients with leptospirosis at a tertiary teaching hospital in Jamaica. Res Rep Trop Med. 2010 Nov;59. doi:10.2147/RRTM.S14118
8. Levett PN. Leptospirosis. Clin Microbiol Rev. 2001 Apr;14(2):296–326. doi:10.1128/CMR.14.2.296-326.2001
9. Shaban L, Toz B, Ramdass A. Workplace- and Residence-Associated Leptospirosis: A Case Report and Review of Current Literature. Cureus. 2022 Oct 3. doi:10.7759/cureus.29879
10. Lizbeth HP, Luis David CH, Saraí PV, Edith RM. Weil's disease: Severe Leptospirosis Cases. Ann Case Rep. 2025 Aug 8;10(4). doi:10.29011/2574-7754.102359
11. Petakh P, Isevych V, Kamyshnyi A, Oksenych V. Weil's Disease—Immunopathogenesis, Multiple Organ Failure, and Potential Role of Gut Microbiota. Biomolecules. 2022 Dec 7;12(12):1830. doi:10.3390/biom12121830
12. Karpagam KB, Ganesh B. Leptospirosis: a neglected tropical zoonotic infection of public health importance—an updated review. Eur J Clin Microbiol Infect Dis. 2020 May;39(5):835–46. doi:10.1007/s10096-019-03797-4
13. Lane AB, Dore MM. Leptospirosis: A clinical review of evidence based diagnosis, treatment and prevention. World J Clin Infect Dis. 2016;6(4):61. doi:10.5495/wjcid.v6.i4.61
14. Haake DA, Levett PN. Leptospirosis in Humans. In: Adler B, editor. Leptospira and Leptospirosis [Internet]. Berlin, Heidelberg: Springer Berlin Heidelberg; 2015 [cited 2026 Jul 16]. p. 65–97. (Current Topics in Microbiology and Immunology). Available from: https://link.springer.com/10.1007/978-3-662-45059-8_5 doi:10.1007/978-3-662-45059-8_5
15. Chou LF, Yang HY, Hung CC, Tian YC, Hsu SH, Yang CW. Leptospirosis kidney disease: Evolution from acute to chronic kidney disease. Biomed J. 2023 Aug;46(4):100595. doi:10.1016/j.bj.2023.100595
16. Daher EDF, Abreu KLSD, Silva Junior GBD. Insuficiência renal aguda associada à leptospirose. J Bras Nefrol. 2010 Dec;32(4):408–15. doi:10.1590/S0101-28002010000400010
17. Tanaka K, Tanabe K, Nishii N, Takiue K, Sugiyama H, Wada J. Sustained Tubulointerstitial Inflammation in Kidney with Severe Leptospirosis. Intern Med. 2017;56(10):1179–84. doi:10.2169/internalmedicine.56.8084
18. Srisawat N, Sitprija V. Leptospirosis and the Kidney: An Overview. In: Yang CW, Pan MJ, Yang HY, editors. Translational Research in Biomedicine [Internet]. S. Karger AG; 2019 [cited 2026 Jul 22]. p. 1–9. Available from: https://karger.com/chapter/doi/10.1159/000500376 doi:10.1159/000500376
19. Araujo ER, Seguro AC, Spichler A, Magaldi AJ, Volpini RA, De Brito T. Acute kidney injury in human leptospirosis: an immunohistochemical study with pathophysiological correlation. Virchows Arch. 2010 Apr;456(4):367–75. doi:10.1007/s00428-010-0894-8
20. Sitprija V. Altered fluid, electrolyte and mineral status in tropical disease, with an emphasis on malaria and leptospirosis. Nat Clin Pract Nephrol. 2008 Feb;4(2):91–101. doi:10.1038/ncpneph0695
21. Siriwanij T, Suttinont C, Tantawichien T, Chusil S, Kanjanabuch T, Sitprija V. Haemodynamics in leptospirosis: Effects of plasmapheresis and continuous venovenous haemofiltration. Nephrology. 2005 Feb;10(1):1–6. doi:10.1111/j.1440-1797.2005.00332.x
22. Lima RSA, da Silva Junior GB, Liborio AB, Daher EDF. Acute kidney injury due to rhabdomyolysis. Saudi J Kidney Dis Transplant Off Publ Saudi Cent Organ Transplant Saudi Arab. 2008 Sep;19(5):721–9. PubMed PMID: 18711286.
23. Delmas B, Jabot J, Chanareille P, Ferdynus C, Allyn J, Allou N, et al. Leptospirosis in ICU: A Retrospective Study of 134 Consecutive Admissions. Crit Care Med. 2018 Jan;46(1):93–9. doi:10.1097/CCM.0000000000002825
24. Andrade LAA, Cleto SAA, Seguro AC. Door-to-Dialysis Time and Daily Hemodialysis in Patients with Leptospirosis: Impact on Mortality. Clin J Am Soc Nephrol. 2007 Jul;2(4):739–44. doi:10.2215/CJN.00680207
25. Gaudry S, Hajage D, Schortgen F, Martin-Lefevre L, Pons B, Boulet E, et al. Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit. N Engl J Med. 2016 Jul 14;375(2):122–33. doi:10.1056/NEJMoa1603017
26. The STARRT-AKI Investigators. Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury. N Engl J Med. 2020 Jul 16;383(3):240–51. doi:10.1056/NEJMoa2000741
27. Barbar SD, Clere-Jehl R, Bourredjem A, Hernu R, Montini F, Bruyère R, et al. Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis. N Engl J Med. 2018 Oct 11;379(15):1431–42. doi:10.1056/NEJMoa1803213

28. Julien M, Rafat C, Raffray L, Vacher-Coponat H, Allou N, Allyn J, et al. Immediate or delayed initiation of renal replacement therapy in patients with leptospirosis and acute kidney injury: a target trial emulation. Ann Intensive Care. 2025;15(1):65. doi:10.1186/s13613-025-01477-5
29. Rajapakse S. Leptospirosis: clinical aspects. Clin Med. 2022 Jan;22(1):14–7. doi:10.7861/clinmed.2021-0784
30. Smith S, Liu YH, Carter A, Kennedy BJ, Dermedgoglou A, Poulgrain SS, et al. Severe leptospirosis in tropical Australia: Optimising intensive care unit management to reduce mortality. Vinetz JM, editor. PLoS Negl Trop Dis. 2019 Dec 2;13(12):e0007929. doi:10.1371/journal.pntd.0007929
31. Faucher JF, Hoen B, Estavoyer JM. The management of leptospirosis. Expert Opin Pharmacother. 2004 Apr;5(4):819–27. doi:10.1517/14656566.5.4.819
32. Sitprija V, Losuwanrak K, Kanjanabuch T. Leptospiral Nephropathy. Semin Nephrol. 2003 Jan;23(1):42–8. doi:10.1053/snep.2003.50004
33. Pongpan S, Thanatrakolsri P, Vittaporn S, Khamnuan P, Daraswang P. Prognostic Factors for Leptospirosis Infection Severity. Trop Med Infect Dis. 2023 Feb 11;8(2):112. doi:10.3390/tropicalmed8020112